What is claimed is:

1. A method of profiling the genomic regulatory regions of a biological sample, comprising:

(1) contacting a sample of nucleic acid from a biological sample, with a positionally addressable array of polynucleotides under conditions such that hybridization can occur, said sample of nucleic acid being enriched in ACEs or fragments thereof of at least 10 base pairs; and

(2) detecting loci on the array where hybridization occurs,

wherein said ACEs are each a nucleotide sequence characterized as being hypersensitive to a DNA modifying agent relative to a nearby region when present in chromatin isolated from one or more cells, has a size in the range of 80-250 base pairs, and is bound by one or more sequence-specific DNA binding factors when present in chromatin isolated from one or more cells,

and wherein said array of polynucleotides comprises a plurality of polynucleotides, each affixed to a substrate, said plurality comprising different polynucleotides differing in nucleotide sequence and being situated at distinct loci of the array, said different polynucleotides being complementary and hybridizable to genomic DNA of said biological sample,

thereby profiling the genomic regulatory regions of the biological sample.

2. The method of claim 1, wherein said plurality of polynucleotides is at least 500 different polynucleotides, at least 1,000 different polynucleotides, at least 5,000 different polynucleotides, at least 10,000 different polynucleotides, or at least 20,000 different polynucleotides.

3. The method of claim 1, wherein each said ACE is further characterized as having one or more of the following characteristics:

(1) an intrinsic ability to confer hypersensitivity to the DNA modifying agent when excised from its native location and inserted into at least one different location in the genome of a cell of the same cell type;

(2) a greater hypersensitivity to the DNA modifying agent relative to the nearby region, wherein said hypersensitivity is 10-50 times greater hypersensitivity, 50-100 times greater hypersensitivity, 100-150 times greater hypersensitivity or 150-200 times greater hypersensitivity to the DNA modifying agent relative to the nearby region;

(3) the ability to reconstitute a site that is hypersensitive to the DNA modifying agent when a nucleic acid comprising the nucleotide sequence flanked by at least 1000 bp on each side is assembled into chromatin in an *in vitro* reconstitution assay in the presence of nucleosomal proteins and a cell extract;

(4) is non-nucleosomal when present in chromatin isolated from one or more cells;

(5) is embedded in DNA associated with histones that have a high degree of acetylation when present in chromatin isolated from one or more cells;

(6) greater solubility than nucleosomal material in moderate salt solutions (e.g., 150 mM NaCl and 3mM $MgCl_2$) when present in chromatin isolated from one or more cells;

(7) is a non-coding sequence; or

(8) does not occur greater than 10 times in a genome of the organism in which the ACE is identified.

4. A positionally addressable polynucleotide array comprising a plurality of different polynucleotides, each different polynucleotide (a) differing in nucleotide

sequence, (b) being affixed to a substrate at a different locus, (c) being in the range of 10-1000 nucleotides in length, and (d) being complementary and hybridizable to a predetermined ACE, each said ACE being a nucleotide sequence characterized as being hypersensitive to a DNA modifying agent relative to a nearby region when present in chromatin isolated from one or more cells, has a size in the range of 80-250 base pairs, and is bound by one or more sequence-specific DNA binding factors when present in chromatin isolated from one or more cells, and

wherein the loci at which said different polynucleotides are situated are at least 15% of the total loci of the array.

5. The positionally addressable polynucleotide array of claim 4 in which each different polynucleotide is greater than 30 nucleotides and is designed so as not to contain a sequence of in the range of 15-30 nucleotides that occurs in the genome of the organism from which the ACEs are identified greater than 10 times.

6. The positionally addressable polynucleotide array of claim 5, wherein each said different polynucleotide is designed by a method comprising

(a) identifying by comparing to an indexed polynucleotide set a sequence in said different polynucleotide, wherein said sequence consists of a nucleotide sequence in the range of 10-15 nucleotides and has a frequency count less than 11 in the genome of said organism, and wherein said indexed polynucleotide set contains binary encoded nucleotide sequences of sizes in the range of 10-15 nucleotides;

(b) determining the genomic locations of said sequence from said indexed polynucleotide set;

(c) adding prefix and suffix nucleotide sequences to said sequence according to the genomic sequence at each of said genomic locations to generate a set of candidate polynucleotides; and

(d) accepting a polynucleotide from said set of candidate polynucleotides if the respective alignment of the sequences of its added prefix and suffix sequences and the

prefix and suffix sequences of said sequence in the corresponding predetermined ACE is above a given threshold.

7. A positionally addressable polynucleotide array to which nucleic acids are hybridized, said array comprising a plurality of different polynucleotides, each different polynucleotide (a) differing in nucleotide sequence and (b) being affixed at a different locus to a substrate, said nucleic acids being enriched in ACEs or fragments thereof of at least 10 base pairs, each said ACE being a nucleotide sequence characterized as being a nucleotide sequence characterized as being hypersensitive to a DNA modifying agent relative to a nearby region when present in chromatin isolated from one or more cells, has a size in the range of 80-250 base pairs, and is bound by one or more sequence-specific DNA binding factors when present in chromatin isolated from one or more cells, said nucleic acids being hybridized to one or more discrete loci on the array.

8. A positionally addressable polynucleotide array to which nucleic acids are hybridized, said array comprising a plurality of different polynucleotides, each different polynucleotide (a) differing in nucleotide sequence, (b) being affixed at a different locus to a substrate, (c) being in the range of 10-1000 nucleotides in length, and (d) being complementary and hybridizable to a predetermined ACE, each said ACE being a nucleotide sequence characterized as being a nucleotide sequence characterized as being hypersensitive to a DNA modifying agent relative to a nearby region when present in chromatin isolated from one or more cells, has a size in the range of 80-250 base pairs, and is bound by one or more sequence-specific DNA binding factors when present in chromatin isolated from one or more cells, and

wherein the loci at which said different polynucleotides are situated are at least 15% of the total loci of the array.

9. A positionally addressable polynucleotide array to which nucleic acids are hybridized, said array comprising a plurality of different polynucleotides, each different polynucleotide (a) differing in nucleotide sequence, (b) being affixed at a different locus

to a substrate, (c) being in the range of 10-1000 nucleotides in length, and (d) being complementary and hybridizable to a predetermined ACE, each said ACE being a nucleotide sequence characterized as said ACE being a nucleotide sequence characterized as being hypersensitive to a DNA modifying agent relative to a nearby region when present in chromatin isolated from one or more cells, has a size in the range of 80-250 base pairs, and is bound by one or more sequence-specific DNA binding factors when present in chromatin isolated from one or more cells,

wherein the loci at which said different polynucleotides are situated are at least 15% of the total loci of the array;

and wherein said nucleic acids are enriched in ACEs or fragments thereof of at least 10 base pairs.

10. The positionally addressable polynucleotide array of claim 4, 7, 8, or 9, wherein said plurality of polynucleotides is at least 500 different polynucleotides, at least 1,000 different polynucleotides, at least 5,000 different polynucleotides, at least 10,000 different polynucleotides, or at least 20,000 different polynucleotides.

11. The positionally addressable polynucleotide array of claim 4, 7, 8, or 9, wherein each said ACE is further characterized as having one or more of the following characteristics:

(1) an intrinsic ability to confer hypersensitivity to the DNA modifying agent when excised from its native location and inserted into at least one different location in the genome of a cell of the same cell type;

(2) a greater hypersensitivity to the DNA modifying agent relative to a nearby region, wherein said hypersensitivity is 10-50 times greater hypersensitivity, 50-100 times greater hypersensitivity, 100-150 times greater hypersensitivity or 150-200 times greater hypersensitivity to the DNA modifying agent relative to the nearby region;

(3) the ability to reconstitute a site that is hypersensitive to the DNA modifying agent when a nucleic acid comprising the nucleotide sequence flanked by at least 1000 bp on each side is assembled into chromatin in an *in vitro* reconstitution assay in the presence of nucleosomal proteins and a cell extract;

(4) is non-nucleosomal when present in chromatin isolated from one or more cells;

(5) is embedded in DNA associated with histones that have a high degree of acetylation when present in chromatin isolated from one or more cells;

(6) greater solubility than nucleosomal material in moderate salt solutions (e.g., 150 mM NaCl and 3mM $MgCl_2$) when present in chromatin isolated from one or more cells;

(7) is a non-coding sequence; or

(8) does not occur greater than 10 times in a genome of the organism in which the ACE is identified.

12. A method for profiling chromatin sensitivity of a genomic region of cells of a cell type to digestion by a DNA modifying agent, comprising determining a chromatin sensitivity profile, said chromatin sensitivity profile comprising a plurality of replicate measurements of each of a plurality of different genomic sequences in said genomic region, wherein each of said plurality of replicate measurements is a ratio of (i) the intensity of signal of a test probe made from a treated cell type following hybridization to a microarray and (ii) the intensity of hybridization of a reference probe of said cell type that has not been treated with said DNA modifying agent.

13. The method of claim 12, wherein said plurality of different genomic sequences comprises successively overlapping sequences tiled across one or more portions of said genomic region.

14. The method of claim 13, wherein said plurality of different genomic sequences comprises successively overlapping sequences tiled across said genomic region.

15. The method of claim 12, wherein each of said plurality of different genomic sequences has a length in the range of about 75 to about 300 bases.

16. The method of claim 15, wherein said plurality of different genomic sequences comprises successively overlapping sequences tiled across said genomic region.

17. The method of claim 12, wherein each of said plurality of different genomic sequences has a length in the range of about 25 to about 80 bases.

18. The method of claim 17, wherein the mean length of said plurality of different genomic sequences is about 40 bases.

19. The method of claim 12, wherein said plurality of duplicate measurements consists of at least 3 duplicate measurements.

20. The method of claim 19, wherein said plurality of duplicate measurements consists of at least 6 duplicate measurements.

21. The method of claim 20, wherein said plurality of duplicate measurements consists of at least 9 duplicate measurements.

22. The method of claim 12, further comprising determining a baseline chromatin sensitivity profile by a method comprising

(a) smoothing the data in said chromatin sensitivity profile to obtain a baseline curve; and

(b) determining the error bounds for said baseline curve,

wherein said baseline curve and said error bounds constitute said baseline chromatin profile.

23. The method of claim 22, wherein said smoothing is carried out using LOWESS.

24. The method of claim 22, wherein said error bounds are determined by a method comprising

(b1) mean centering said plurality of replicates for each genomic sequence in said chromatin sensitivity profile about said baseline curve to generate a mean-centered chromatin sensitivity profile, wherein said mean-centering is carried out by setting the mean of each said plurality of replicates to the value of the corresponding genomic sequence on said baseline curve;

(b2) determining the median M of said mean-centered chromatin sensitivity profile;

(b3) determining the Median Average Deviation MAD of said mean-centered chromatin sensitivity profile;

(b4) discarding for each genomic sequence replicate measurement X if X satisfy equation

$$\frac{|X-M|}{MAD/0.6745} > 2.24$$, and

(b5) defining the error bounds as the lower and upper confidence limits on the remaining data.

25. The method of claim 22, wherein said error bounds are determined by a method comprising

(b1) generating a bootstrap chromatin sensitivity profile by randomly selecting one replicate measurement from said plurality of replicate measurements for each genomic sequence;

(b2) mean centering said plurality of replicates for each genomic sequence in said bootstrap chromatin sensitivity profile about said baseline curve to generate a mean-centered chromatin sensitivity profile, wherein said mean-centering is

carried out by setting the mean of each said plurality of replicates to the value of the corresponding genomic sequence on said baseline curve;

(b3) determining the median M of said mean-centered chromatin sensitivity profile;

(b4) determining the Median Average Deviation MAD of said mean-centered chromatin sensitivity profile;

(b5) discarding for each genomic sequence replicate measurement X if X satisfy equation

$$\frac{|X-M|}{MAD/0.6745} > 2.24,$$

(b5) determining the maximum lower and minimum upper outliers on the remaining data;

(b6) repeating said step (b1)-(b5) for a plurality of times; and

(b7) calculating the upper and lower outlier cutoff values and Bca confidence intervals.

26. The method of claims 24, further comprising

(c1) identifying one or more genomic sequences among said plurality of genomic sequences whose 20% trimmed means lie outside said error bounds; and

(c2) determining a signal-to-noise ratio S/N of said identified genomic sequences according to equation

$$S/N_i = \frac{|HS_i - B_i|}{MAD_B(\sigma_c/\sigma_{HS})^2}$$

where S/N_i is the signal-to-noise ratio at site i, HS_I is the Y% trimmed mean of the corresponding HS cluster, B_I is the value of said baseline curve at said site *i*, MAD_B is the median average deviation of the centered baseline, σ_{HS} is the average variance of replicate measurements, and σ_c is the variance of the replicate measurements at said site *i*.

27. The method of claims 25, further comprising

(c1) identifying one or more genomic sequences among said plurality of genomic sequences whose 20% trimmed means lie outside said error bounds; and

(c2) determining a signal-to-noise ratio S/N of said identified genomic sequences according to equation

$$S/N_i = \frac{|HS_i - B_i|}{MAD_B(\sigma_c/\sigma_{HS})^2}$$

where S/N_i is the signal-to-noise ratio at site i, HS_i is the Y% trimmed mean of the corresponding HS cluster, B_i is the value of said baseline curve at said site *i*, MAD_B is the median average deviation of the centered baseline, σ_{HS} is the average variance of replicate measurements, and σ_c is the variance of the replicate measurements at said site *i*.

28. The method of any one of claims 12-27, wherein each said copy number has been corrected for amplification efficiency.

29. The method of any one of claims 12-27, wherein said DNA modifying agent is DNase I.

30. The method of any one of claims 12-27, wherein each of said plurality of duplicated measurements is measured by independent microarray hybridization experiments.

31. The method of any one of claims 12-27, wherein each of said plurality of duplicated measurements is measured by independent microarray hybridization experiments using different treated chromatin samples.

32. A method for profiling chromatin sensitivity of a genomic region of cells of a cell type to digestion by a DNA modifying agent, comprising

(a) treating chromatin of cells of said cell type with said DNA modifying agent such that digestion of DNA occurs and retrieving DNA molecules;

(b) creating Test probes by various methods from chromatin of cells of said type treated by said DNA modifying agent;

(c) creating Reference probes by various methods from chromatin of cells of said type untreated by said DNA modifying agent;

(d) determining a ratio of intensity of hybridization signal of probes described in step (b) and step (c) following hybridization to a microarray;

(e) repeating said steps (b) - (d) a plurality of times to generate a plurality of ratios, thereby generating a plurality of replicate measurements for each of said genomic sequences; and

(d) determining a chromatin sensitivity profile of said genomic region, said chromatin sensitivity profile comprising said plurality of replicate measurements.

33. The method of claim 32, wherein said plurality of different genomic sequences comprises successively overlapping sequences tiled across one or more portions of said genomic region.

34. The method of claim 33, wherein said plurality of different genomic sequences comprises successively overlapping sequences tiled across said genomic region.

35. The method of claim 32, wherein each of said plurality of different genomic sequences has a length in the range of about 75 to about 300 bases.

36. The method of claim 35, wherein the mean length of said plurality of different genomic sequences is about 250 bases.

37. The method of claim 32, wherein each of said plurality of different genomic sequences has a length in the range of about 25 to about 80 bases.

38. The method of claim 37, wherein the mean length of said plurality of different genomic sequences is about 40 bases.

39. The method of claim 32, wherein said plurality of duplicate measurements consists of at least 3 duplicate measurements.

40. The method of claim 39, wherein said plurality of duplicate measurements consists of at least 6 duplicate measurements.

41. The method of claim 40, wherein said plurality of duplicate measurements consists of at least 9 duplicate measurements.

42. The method of claim 32, further comprising determining a baseline chromatin sensitivity profile by a method comprising

(a) smoothing the data in said chromatin sensitivity profile to obtain a baseline curve; and

(b) determining the error bounds for said baseline curve,

wherein said baseline curve and said error bounds constitute said baseline chromatin profile.

43. The method of claim 42, wherein said smoothing is carried out using LOWESS.

44. The method of claim 42, wherein said error bounds are determined by a method comprising

(b1) mean centering said plurality of replicates for each genomic sequence in said chromatin sensitivity profile about said baseline curve to generate a mean-centered chromatin sensitivity profile, wherein said mean-centering is carried out by setting the mean of each said plurality of replicates to the value of the corresponding genomic sequence on said baseline curve;

(b2) determining the median M of said mean-centered chromatin sensitivity profile;

(b3) determining the Median Average Deviation MAD of said mean-centered chromatin sensitivity profile;

(b4) discarding for each genomic sequence replicate measurement X if X satisfy equation

$$\frac{|X-M|}{MAD/0.6745} > 2.24, \text{ and}$$

(b5) defining the error bounds as the lower and upper confidence limits on the remaining data.

45. The method of claim 42, wherein said error bounds are determined by a method comprising

(b1) generating a bootstrap chromatin sensitivity profile by randomly selecting one replicate measurement from said plurality of replicate measurements for each genomic sequence;

(b2) mean centering said plurality of replicates for each genomic sequence in said bootstrap chromatin sensitivity profile about said baseline curve to generate a mean-centered chromatin sensitivity profile, wherein said mean-centering is carried out by setting the mean of each said plurality of replicates to the value of the corresponding genomic sequence on said baseline curve;

(b3) determining the median M of said mean-centered chromatin sensitivity profile;

(b4) determining the Median Average Deviation MAD of said mean-centered chromatin sensitivity profile;

(b5) discarding for each genomic sequence replicate measurement X if X satisfy equation

$$\frac{|X-M|}{MAD/0.6745} > 2.24,$$

(b5) determining the maximum lower and minimum upper outliers on the remaining data;

(b6) repeating said step (b1)-(b5) for a plurality of times; and

(b7) calculating the upper and lower outlier cutoff values and Bca confidence intervals.

46. The method of claims 44, further comprising

(c1) identifying one or more genomic sequences among said plurality of genomic sequences whose 20% trimmed means lie outside said error bounds; and

(c2) determining a signal-to-noise ratio S/N of said identified genomic sequences according to equation

$$S/N_i = \frac{|HS_i - B_i|}{MAD_B(\sigma_c/\sigma_{HS})^2}$$

where S/N_i is the signal-to-noise ratio at site i, HS_i is the Y% trimmed mean of the corresponding HS cluster, B_i is the value of said baseline curve at said site *i*, MAD_B is the median average deviation of the centered baseline, σ_{HS} is the average variance of replicate measurements, and σ_c is the variance of the replicate measurements at said site *i*.

47. The method of claims 44, further comprising

(c1) identifying one or more genomic sequences among said plurality of genomic sequences whose 20% trimmed means lie outside said error bounds; and

(c2) determining a signal-to-noise ratio S/N of said identified genomic sequences according to equation

$$S/N_i = \frac{|HS_i - B_i|}{MAD_B(\sigma_c/\sigma_{HS})^2}$$

where S/N_i is the signal-to-noise ratio at site i, HS_i is the Y% trimmed mean of the corresponding HS cluster, B_i is the value of said baseline curve at said site *i*, MAD_B is the median average deviation of the centered baseline, σ_{HS} is the average variance of replicate measurements, and σ_c is the variance of the replicate measurements at said site *i*.

48. The method of any one of claims 32-47, wherein each said hybridization intensity has been normalised.

49. The method of any one of claims 32-48, wherein said DNA modifying agent is DNase I.

50. The method of any one of claims 32-47, wherein each of said plurality of duplicated measurements is measured by independent microarray hybridization experiments.

51. The method of any one of claims 32-47, wherein each of said plurality of duplicated measurements is measured by independent microarray hybridization experiments using different treated chromatin samples.

52. The method of any one of claims 26-27 and 46-47, wherein said Y% trimmed mean is 20% trimmed mean.